UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,110	09/11/2003	Mark F. Oldham	ABIOS.041A	6842

20995 7590 03/02/2007	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP	NEGIN, RUSSELL SCOTT	
2040 MAIN STREET		
FOURTEENTH FLOOR	ART UNIT	PAPER NUMBER
IRVINE, CA 92614	1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	03/02/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 03/02/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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PTOL-90A (Rev. 10/06)

	Application No.	Applicant(s)
Office Action Summary	10/660,110	OLDHAM ET AL.
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE **3** MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on <u>05 December 2006</u>.

2a)☒ This action is **FINAL**.   2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) <u>20-44</u> is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) <u>20-44</u> is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All   b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
    Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
    Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Specification

The objection to the disclosure because of the following informalities is withdrawn

due to amendments made by applicant to the set of claims filed on 5 December 2006.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on
sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20-24 and 33-36 are rejected under 35 U.S.C. 102(b) as being

anticipated by Morris [Nuclear Magnetic Resonance Imaging in Medicine and Biology,

1986, Oxford: Clarendon Press].

Claims 20-24 and 33-36 state:

20. A method for improving the measurement of one or more types of specific particles
of a sample using a detector associated with a biological analysis system wherein the
specific particles are adapted to emit identifiable signals based on the interaction of the
specific particles with corresponding probes and wherein the identifiable signals are
captured by the detector to yield an output signal and wherein the detector is adapted to
be operated at different configurations that respond differently to the identifiable signals,
the method comprising: performing a first measurement of the identifiable signals with
the detector at a first configuration such that the detector yields a first output signal
wherein the first configuration allows effective measurement of a first type of the specific
particles, wherein the first configuration includes a first operating parameter of the
detector; performing a second measurement of the identifiable signals with the detector
at a second configuration such that the detector yields a second output signal wherein
the second configuration allows effective measurement of the second type of the
specific particles, wherein the second configuration includes a second operating
parameter of the detector; and adjusting one of the first and second output signals
based on a relationship between the first and second parameters to obtain a
representation of the identifiable signals wherein the representation of the identifiable
signals includes effective representations of the first and second types of the specific
particles to thereby allow improved identification of the specific particles within the
sample.

21. The method of claim 20, wherein the first measurement at the first configuration is adapted to effectively measure a relatively strong component of the identifiable signals associated with the first type of the specific particles having a relatively high abundance.

22. The method of claim 21, wherein the second measurement at the second configuration is adapted to effectively measure a relatively weak component of the identifiable signals associated with the second type of the specific particles having a relatively low abundance.

23. The method of claim 22, wherein combining the first and second output signals comprises scaling the first output signal to a scale associated with the second configuration such that the based on the second configuration, the weak component is effectively measured and the strong component is effectively represented based on the scaling of the effectively measured value from the first configuration.

24. The method of claim 23, wherein the scaling of the strong component allows effective representation of both weak and strong components when a dynamic range associated with the detector is limited and would not be able to measure the strong component at the second configuration.

33. A method extending the effective dynamic range of a detector that measures detectable signals from a sample undergoing a biological analysis wherein the detectable signals comprise two or more components representative of two or more components of the sample, the method comprising: obtaining a first output signal from the detector operated at a first configuration that allows effective measurement of a first component of the detectable signals; obtaining a second output signal from the detector operated at a second configuration that allows effective measurement of a second component of the detectable signals wherein the second configuration is such that the first component of the detectable signals would fall outside the detector's dynamic range at the second configuration; and scaling the first output signal to a scale associated with the second configuration wherein the amount of scaling depends on the first and second configurations and wherein the scaled first output signal allows representation of the first output signal at the second configuration thereby extending the effective dynamic range of the detector and wherein such extension of the effective dynamic range allows improved characterization of the sample having a relatively large range of relative abundances of the two or more components.

34. The method of claim 33, wherein the first configuration is adapted to effectively measure a strong component of the detectable signals.

35. The method of claim 34, wherein the second configuration is adapted to effectively measure a weak component of the detectable signals.

36. The method of claim 35, wherein scaling the first output signal allows representation of both weak and strong components when the dynamic range associated with the detector is limited and would not be able to measure the strong component at the second configuration.

The technique that anticipates the instantly rejected set of claims is quadrature detection in Nuclear Magnetic Resonance.

Morris explains quadrature detection in section 2.4.2.3 of his book on pages 32-35. In the spectrometer, quadrature detection is used for determining the direction of nuclear precision and to enhance signal to noise ratios. As explained on the first line of page 34, "In practice, one normally employs two p.s.d.s [phase sensitive detectors] with reference phases in quadrature (90° apart). This method is known as quadrature detection and is desirable since it allows a $\sqrt{2}$ improvement in S/N to be achieved..." Consequently, the operating parameter of the first detector is the angle at which it observes the signals and the operating parameter of the second detector is the second angle at which the signals are observed (a shift of 90° from the initial operating parameter or signal). This factor of $\sqrt{2}$ enforces a scaling of the amplitude of the instant signals. The two phase sensitive detectors are synchronized to act as a single device used to transmit a single signal and spectrum.

Figure 2.11 on page 34 of Morris illustrates a signal detection device in a configuration along the x-axis used to deliver a first measurement of the identifiable signal. The initial measurement along the x-axis yields a high abundance as shown in Figure 2.11.

Figure 2.11 of page 34 of Morris illustrates a signal detection device in a

configuration along the y axis used to deliver a second measurement of the identifiable

signal. The initial measurement along the y-axis yields a low abundance as shown in

Figure 2.11.

The synchronization and combination of these signals yields a more strongly

scaled single signal as a result of the dual method of detection with improved signal to

noise ratios.

The types of particles measured are nuclei of atoms and are "nuclear spin

systems" (page 32 of Morris, third line from the bottom).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in
section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are
such that the subject matter as a whole would have been obvious at the time the invention was made to a
person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived
by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of

the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g)

prior art under 35 U.S.C. 103(a).

35 U.S.C. 103 Rejection #1:

Claims 20-30 and 33-42 are rejected under 35 U.S.C. 103(a) as being

unpatentable over Morris in view of Churchill et al. [IEEE Transactions on Aerospace

and Electronic Systems, Volume AES-17, no. 1, 1981] in view of Pierre et al. [IEEE

Transactions on Aerospace and Electronic Systems, 1995 pages 1900-1902] in view of

Tacklind et al. [US PGPUB 2003/0101605 A1].

20. A method for improving the measurement of one or more types of specific particles
of a sample using a detector associated with a biological analysis system wherein the
specific particles are adapted to emit identifiable signals based on the interaction of the
specific particles with corresponding probes and wherein the identifiable signals are
captured by the detector to yield an output signal and wherein the detector is adapted to
be operated at different configurations that respond differently to the identifiable signals,
the method comprising: performing a first measurement of the identifiable signals with
the detector at a first configuration such that the detector yields a first output signal
wherein the first configuration allows effective measurement of a first type of the specific
particles, wherein the first configuration includes a first operating parameter of the
detector; performing a second measurement of the identifiable signals with the detector
at a second configuration such that the detector yields a second output signal wherein
the second configuration allows effective measurement of the second type of the
specific particles, wherein the second configuration includes a second operating
parameter of the detector; and adjusting one of the first and second output signals
based on a relationship between the first and second parameters to obtain a
representation of the identifiable signals wherein the representation of the identifiable
signals includes effective representations of the first and second types of the specific
particles to thereby allow improved identification of the specific particles within the
sample.

21. The method of claim 20, wherein the first measurement at the first configuration is
adapted to effectively measure a relatively strong component of the identifiable signals
associated with the first type of the specific particles having a relatively high abundance.

22. The method of claim 21, wherein the second measurement at the second

configuration is adapted to effectively measure a relatively weak component of the identifiable signals associated with the second type of the specific particles having a relatively low abundance.

23. The method of claim 22, wherein combining the first and second output signals comprises scaling the first output signal to a scale associated with the second configuration such that the based on the second configuration, the weak component is effectively measured and the strong component is effectively represented based on the scaling of the effectively measured value from the first configuration.

24. The method of claim 23, wherein the scaling of the strong component allows effective representation of both weak and strong components when a dynamic range associated with the detector is limited and would not be able to measure the strong component at the second configuration.

25. The method of claim 24, wherein the detector is a charge-coupled device and the first configuration comprises a short exposure duration T1 selected to effectively measure the strong component of the identifiable signals.

26. The method of claim 25, wherein the second configuration comprises a long exposure duration T2 selected to effectively measure a weak component of the identifiable signals.

27. The method of claim 26, wherein the scaling of the first output signal comprises multiplying the first output signal value by a ratio T2/T1.

28. The method of claim 24, wherein the detector is a charge multiplier and the first configuration comprises a low operating voltage V1 selected to effectively measure the strong component of the identifiable signals.

29. The method of claim 28, wherein the second configuration comprises a high operating voltage V2 selected to effectively measure a weak component of the identifiable signals.

30. The method of claim 29, wherein the scaling of the first output signal comprises determining the scaled value N1' of the first output signal based on a relationship $\log(N1')=m \log(V2/V1)$ where m represents a slope of a curve obtained by plotting the multiplier's gain versus the voltage in a log-log manner.

33. A method extending the effective dynamic range of a detector that measures detectable signals from a sample undergoing a biological analysis wherein the detectable signals comprise two or more components representative of two or more components of the sample, the method comprising: obtaining a first output signal from the detector operated at a first configuration that allows effective measurement of a first

component of the detectable signals; obtaining a second output signal from the detector operated at a second configuration that allows effective measurement of a second component of the detectable signals wherein the second configuration is such that the first component of the detectable signals would fall outside the detector's dynamic range at the second configuration; and scaling the first output signal to a scale associated with the second configuration wherein the amount of scaling depends on the first and second configurations and wherein the scaled first output signal allows representation of the first output signal at the second configuration thereby extending the effective dynamic range of the detector and wherein such extension of the effective dynamic range allows improved characterization of the sample having a relatively large range of relative abundances of the two or more components.

34. The method of claim 33, wherein the first configuration is adapted to effectively measure a strong component of the detectable signals.

35. The method of claim 34, wherein the second configuration is adapted to effectively measure a weak component of the detectable signals.

36. The method of claim 35, wherein scaling the first output signal allows representation of both weak and strong components when the dynamic range associated with the detector is limited and would not be able to measure the strong component at the second configuration.

37. The method of claim 36, wherein the detector is a charge-coupled device and the first configuration comprises a short exposure duration T1 selected to effectively measure the strong component of the detectable signals.

38. The method of claim 37, wherein the second configuration comprises a long exposure duration T2 selected to effectively measure a weak component of the detectable signals.

39. The method of claim 38, wherein the scaling of the first output signal comprises multiplying the first output signal value by a ratio T2/T1.

40. The method of claim 36, wherein the detector is a charge multiplier and the first configuration comprises a low operating voltage V1 selected to effectively measure the strong component of the detectable signals.

41. The method of claim 40, wherein the second configuration comprises a high operating voltage V2 selected to effectively measure a weak component of the detectable signals.

42. The method of claim 41, wherein the scaling of the first output signal comprises determining the scaled value N1' of the first output signal based on a relationship

log(N1')=m log(V2/V1) where m represents a slope of a curve obtained by plotting the
multiplier's gain versus the voltage in a log-log manner.

The technique that describes the instantly rejected set of claims is quadrature
detection in Nuclear Magnetic Resonance.

Morris explains quadrature detection in section 2.4.2.3 of his book on pages 32-
35. In the spectrometer, quadrature detection is used for determining the direction of
nuclear precision and to enhance signal to noise ratios. As explained on the first line of
page 34, "In practice, one normally employs two p.s.d.s [phase sensitive detectors] with
reference phases in quadrature (90° apart). This method is known as quadrature
detection and is desirable since it allows a √2 improvement in S/N to be achieved..."
Consequently, the operating parameter of the first detector is the angle at which it
observes the signals and the operating parameter of the second detector is the second
angle at which the signals are observed (a shift of 90° from the initial operating
parameter or signal). This factor of √2 enforces a scaling of the amplitude of the instant
signals. The two phase sensitive detectors are synchronized to act as a single device
used to transmit a single signal and spectrum.

Figure 2.11 on page 34 of Morris illustrates a signal detection device in a
configuration along the x-axis used to deliver a first measurement of the identifiable
signal. The initial measurement along the x-axis yields a high abundance as shown in
Figure 2.11.

Figure 2.11 of page 34 of Morris illustrates a signal detection device in a
configuration along the y axis used to deliver a second measurement of the identifiable

signal. The initial measurement along the y-axis yields a low abundance as shown in Figure 2.11.

The synchronization and combination of these signals yields a more strongly scaled single signal as a result of the dual method of detection with improved signal to noise ratios.

The types of particles measured are nuclei of atoms and are "nuclear spin systems" (page 32 of Morris, third line from the bottom).

Morris fails to take ratios of these times, show specific voltages employed to regulate the quadrature detector, show the required logarithmic plots, and utilize a charge-coupled device.

Churchill et al. states in the article, "The Correction of I and Q Errors in a Coherent Processor," "A method is presented for correcting the gain and phase imbalances and the bias errors of the in-phase and quadrature channels of a coherent signal processor... The residual errors after correction depend upon the signal-to-noise ratio (S/N) of the test signal and the degree of filtering used in deriving the correction coefficients." The image powers used in the correction of the image power (amplitude and phase) imbalances are shown in the middle of the second column of page 131 and apply to both channels.

However, Churchill et al. fails to manipulate the power values in a method consistent with the requirements of the instant claims or teach the use of a CCD device.

In the article of Pierre et al., entitled, "Considerations in the autocalibration of quadrature receivers," Figure 2 on page 1902 shows a log-log plot of the variance of the

signal to noise ratio as a function of the ratio of two times. The plotted data simulates a line with a specific slope.

However none of the above sources show use of charge coupled devices in signal detection.

Tacklind et al., in their invention entitled, "Servo-controlled automatic level and plumb tool," explain that quadrature detectors and charge coupled devices are interchangeable (paragraph [0060]):

> The position sensitive photo sensor 131 can incorporate any of a number of commercially available position sensitive detectors sensitive to the detector light 134. Examples include, but are not limited to, quadrature detectors, charged coupled devices (CCD) detectors, complementary metal oxide semiconductor (CMOS) image sensors...

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quadrature detection method of Morris in view of the voltage determination method of Churchill et al. in view of the autocalibration method of Pierre et al. in view of the CCD substitution method of Tacklind et al. because while Morris teaches how quadrature detection applies to NMR, Churchill et al. teaches how image power could be used for correction of imbalances in quadrature detection, Pierre et al. teaches how log-log plots correct for considerations in the autocalibration of quadrature receivers, and Tacklind et al. teach how charge coupled devices and replaceable by quadrature detectors for an analogous application. It would be an obvious mathematical transformation to plot voltage or power ratios as determined in Churchill et al. in place of the ratio of times found in Pierre et al. as the two types of plotting techniques are art accepted equivalents.

35 U.S.C. 103 Rejection #2:

Claims 20-24, 28-36, and 40-44 are rejected under 35 U.S.C. 103(a) as being

unpatentable over Morris in view of Churchill et al. in view of Pierre et al. in view of

Tacklind et al. as applied to claims 22-30 and 33-42 above in further view of

Photomultiplier Tubes [Hamamatsu Brochure, pages 1-15, July 2002].

Claims 31-32 and 43-44 state:

31. The method of claim 30, wherein the charge multiplier comprises a photomultiplier
tube.

32. The method of claim 30, wherein the charge multiplier comprises a charge
intensifier.

43. The method of claim 42, wherein the charge multiplier comprises a photomultiplier
tube.

44. The method of claim 42, wherein the charge multiplier comprises a charge
intensifier.

Morris in view of Churchill et al. in view of Pierre et al. in view of Tacklind et al. as

applied to claims 20-30 and 33-42 above do not disclose the photomultiplier tube or the

charge intensifier.

The catalog "Photomultipler tubes" discusses uses and sales of photomultiplier

tubes and charge intensifiers throughout the brochure.

It would have been obvious at the time of the instant invention for someone of

ordinary skill in the art to modify the quadrature detection method of Morris in view of

Churchill et al. in view of Pierre et al. in view of Tacklind et al. as applied to claims 20-30

and 33-42 above in further view of Photomultiplier to result in the instant invention

because Photomuliplier has the advantage of selling the relevant items necessary to improve the efficiency of the claimed invention.

Response to Arguments

Applicant's arguments filed 5 December 2006 have been fully considered but they are not persuasive.

Applicant has several arguments related to the anticipatory prior art rejection. The first argument is on page 7 of the Remarks of 5 December 2005, which states that while signals are combined in quadrature detection, none of the signals are adjusted.

Applicant next argues is on page 7 of the Remarks of 5 December 2005 by stating that the amended limitation in the independent claim including adjusting the one of two signals based on the relationship between the two signals is not taught in the prior art. In other words Morris does not teach adjustment of the two signals based on the relation between the two signals.

Applicant next argues is on page 7 of the Remarks of 5 December 2005 that the prior art does not teach scaling the output of the first configuration using the information in the second configuration.

In response to the first argument of the applicant, Figure 2.10 of Morris on page 33 illustrates how an initial NMR signal in Figure 2.10a is adjusted by use of a second signal that is in quadrature with the initial signal. This adjustment of the detected signal is displayed in the plot of the detected signal in the right column of Figures 2.10a and 2.10b.

In response to the second argument of the applicant, Figure 2.11 of Morris on page 34 illustrates how a single signal illustrated in the left column of Figure 2.11 is measured by two reference detectors in quadrature illustrated in the middle column of Figure 2.11 in order to derive a single signal in the right column of Figure 2.11a which has its phase adjusted to form the (second) signal in the right column of Figure 2.11b.

In response to the third argument of the applicant, the amplitude (i.e. intensity) of the observed, resultant signal is scaled by a factor of $\sqrt{2}$ in amplitude in response to adjusting the original signal by the second signal measured in quadrature.

Applicants' arguments concerning the obviousness prior art rejections are considered and are not found to be persuasive because they are based in their entireties on the anticipatory prior art rejection being invalid.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later

than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by
facsimile transmission. Papers should be faxed to Technical Center 1600 via the
central PTO Fax Center. The faxing of such pages must conform with the notices
published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61
(November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)).
The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the
examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571)
272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's
Supervisor, Irem Yucel, Supervisory Patent Examiner, can be reached at (571) 272-
0781.

Information regarding the status of the application may be obtained from the
Patent Application Information Retrieval (PAIR) system. Status information for
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RSN
22 February 2007

22 February 2007

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER